REMARKS

Claims 1-10 are pending. Claims 2-9 are canceled. Claims 1 and 10 are amended. No new matter is entered.

Support for Amendments

Support for the amendments can be found in the specification and claims as originally filed. No new matter is entered.

Objections

Claims 7-10 are objected to for improper multiple dependencies and are not further examined at this time. Claims 7-9 are canceled, and claim 10 is amended to remove improper multiple dependencies. Applicants request withdrawal of the objection. Upon withdrawal of the objection, Applicants are entitled to examination of all claims.

Rejection Under 35 USC § 112, 1st paragraph

Claims 1 to 6 are rejected under 35 U.S.C §112, first paragraph, because the Examiner contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims have been amended to incorporate elements from dependent claims obviating this ground of rejection.

Rejection Under 35 USC § 112, 2nd paragraph

Claims 1 to 6 are rejected under 35 USC§112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amended claims obviate this ground of rejection.

Rejection Under 35 USC § 102(b)

Claims 1 to 4 and 6 are rejected under 35 USC§102(b) as being anticipated by Sharfstein et al. (1994) Ann NY Acad. Sci. 745:77-91.

Sharfstein et al. describes that by shifting the phosphate level in the medium from the phosphate starvation condition to the phosphate surplus condition, the accumulation of polyphosphates in an E. coli cell increases, and the rapid increase of the activities of PPK gene product and the moderate decrease of the activities of PPX gene product are observed. As PPK forms an operon with PPX, and PPK and PPX are regulated by the same promoter, it seems unlikely that these changes occur only by the transcriptional regulation. Therefore, an idea in which the accumulation of polyphosphate is used as an indicator of the promoter activity measurement cannot come about only from what is taught in Sharfstein et al. In fact, the purpose of the experiment conducted by Sharfstein et al. was not to monitor gene expression. In the instant invention, since the water surrounding polyphosphate molecules subjected to monitoring is influenced, MRI using 1H-NMR, in which monitoring in real time is possible, can be

performed. However, there is no teching of this point either in Sharfstein et al. Accordingly, the instant invention is not anticipated by Sharfstein et al.

Applicants' amendments to claim 1 incorporating elements of dependent claims including monitoring expression non-destructively in real time obviates this ground of rejection.

Claims 1 and 2 are rejected under 35 USC§102(b) as being anticipated by van Voorthuysen et al. (2000) J. Biotech. 77:65-80.

van Voorthuysen et al. teaches that polyphosphate is produced in a plant as a result of PPK expression, but this is not an experiment conducted for the purpose of monitoring gene expression. In the instant invention, since the water surrounding polyphosphate molecules subjected to monitoring is influenced, MRI using 1H-NMR, in which monitoring in real time is possible, can be performed. However, there is no teaching of this point in van Voorthuysen et al.

Claim 1 has been amended to incorporate original claims 3, 4 and 6, as well as other amendments. Therefore, it is believed that this ground of rejection is moot.

Claims 1, 2 and 6 are rejected under 35 USC§102(b) as being anticipated by Walter et al. (2000) PNAS 97:5151-5155.

There are differences between the instant invention and Walter et al. in that, for example, the molecule subjected to monitoring is "polyphosphate having strand length equal to or less than 50 mer in the mean value" in the present invention, and "phosphoarginine" in Walter et al.

In Walter et al., the peak in MRS of phosphoarginine, which is the molecule subjected to monitoring, is partially overlapped with that of phosphocreatine, a substrate of creatine kinase (see Figs. 3 and 4), so that S/N is inferior. Further, as arginine kinase degrades phosphoarginine as with creatine kinase in ischemic conditions, it is inferred that the gene expression amount cannot be reflected as it is and quantitativity would be poor. This is why quantitativity is not taught in Walter et al. On the contrary, in the instant invention, it is not only superior in S/N but there is also little concern that metabolic control similar to that by creatine kinase might occur.

MRS can be performed but MRI cannot be performed in real time in Walter et al. MRI using 31P-NMR could be performed in Walter et al.(unlike polyphosphate molecule subjected to monitoring in the instant invention, the peaks of phosphocreatine and phosphoarginine are close, therefore it is thought to be extremely difficult to carry out MRI using 31P-NMR in Walter et al.). However, it takes a longer time for imaging, which prevents performing MRI in real time. In Walter et al., since the water surrounding phosphoarginine molecules subjected to monitoring is not influenced, MRI using 1H-NMR, which can performed monitoring in real time, cannot be performed. On the contrary, in the present invention, the water surrounding polyphosphate molecules subjected to monitoring is influenced, which allows performance of MRI using 1H-NMR, which can perform monitoring in real time.

Claim 1 has been amended to incorporate original claims 3 and 4 and other elements obviating this ground of rejection.

Claims 1, 5, and 6 are rejected under 35 USC§102(b) as being anticipated by Gropman A. (2001) Curr. Neurol. Neurosci. Rep. 1:185-94.

Claim 1 has been amended to incorporate original claims 2 and 3 as well as other elements obviating this ground of rejection.

Claims 1 and 5 are rejected under 35 USC§102(b) as being anticipated by Ozawa et al. (2001) Biosci, Biotech, Biochem 65:185-189.

Claim 1 has been amended to incorporate original claims 2 to 4 and 6 as well as other elements obviating this ground of rejection.

Claims 1 and 6 are rejected under 35 USC§102(b) as being anticipated by Koretsky et al. (1996) Proceedings of the 4th Int. Soc. Magnetic. Resonance Med. pg. 69.

Claim 1 has been amended to incorporate original claims 2 to 4 and other elements obviating this ground of rejection.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4439-4023.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4439-4023.

Respectfully submitted,
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Dated: July 24, 2006 By: _____
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